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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,264	06/22/2001	Sean H. Adams	10466/35	8727

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/888,264	ADAMS ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,27-41 and 43-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *41 and 43* is/are allowed.

6)☒ Claim(s) *1,27-38,44-56 and 59-71* is/are rejected.

7)☒ Claim(s) *39,40,57,58,72 and 73* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This Action is in response to the communication filed on 2/2/04. The amendment has been entered. Claims 2-26 and 42 are cancelled. Claims 1, 27-41 and 43-73 are currently pending in the application and are addressed herein.

2. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claim Rejections - 35 USC § 112, first paragraph

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 27-38, 44-56, 59-71 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejected is reiterated below, for convenience.

3. The instant claims are drawn to method of identifying compounds that affect uncoupling and encompass analyzing the expression of polypeptides that have at least 90% or at least 95% sequence identity to a polypeptide encoded by SEQ ID NO: 1 or SEQ ID NO: 2. Therefore, the

claims encompass analyzing the expression of a large genus of polypeptides of which only one species has been adequately described in the specification.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (See MPEP 2100-164)

In the instant case, the Applicants have disclosed SEQ ID NO: 1 and SEQ ID NO: 2 both of which encode the human 2-oxoglutarate carrier protein (OGC). Applicants have identified that human OGC "changes mitochondrial membrane potential" (see p. 3, line 24 of the specification). However, applicants have not identified variants of human OGC which retain the ability to change mitochondrial membrane potential. Specifically, applicants have not described which polypeptides that are at least 90% or at least 95% identical to OGC (but less than 100% identical to OGC) have the ability to change mitochondrial membrane potential. The applicants have not identified which common elements or attributes critical for the polypeptide to have the ability to affect mitochondrial membrane potential. For instance, the critical functional domains which are required for the polypeptide to have an affect on mitochondrial membrane potential have not been identified.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that:

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for a specific protein, as well as method of obtaining it, then conception is not achieved

> until reduction to practice has occurred, that is, until after the gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant case, Applicants have identified SEQ ID NOS: 1-2, which encode human OGC protein which they have shown to have an affect on mitochondrial membrane potential. However, Applicants have not identified any variants of human OGC which would also have an affect on mitochondrial membrane potential and which variants would not have an affect on mitochondrial membrane potential. Therefore, one of ordinary skill in would not be able to envision which variants of human OGC would have an affect on mitochondrial membrane potential and which one would not.

Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any variant polypeptide of human OGC which represent functional variants which have the ability to affect mitochondrial membrane potential, a function critical to the successful completion of the claimed method. Therefore, the claims fail to meet the written description requirement by encompassing polypeptides that are not adequately described in the specification.

4. Additionally, since the claims encompass polypeptides for which there is insufficient written description provided in the specification, one of skill in the art would not know how to make or use the claimed method without performing additional experimentation. Considering

the claims encompass a very large genus of polypeptides (i.e., any polypeptide at least 90% identical or ate least 95% identical to the one encoded by SEQ ID NO: 1 or SEQ ID NO: 2) and the fact that one of skill in the art could not readily predict which variants that meet the limitations would have the desired ability to affect mitochondrial membrane potential, the mount of additional experimentation required to identify the functional variants is considered to be undue.

Response to Arguments

5. Applicant's arguments filed 2/2/04 have been fully considered but they are not persuasive. Applicants argue that analyzing for expression does not require making or selecting the polypeptides, only measuring their expression (see p. 9 of the response filed 2/2/04). The Applicants argue that the specification provides a description of methods for measuring the polypeptides encompassed by the claims. Applicants contend that they are NOT claiming the polypeptides that are 90% or more identical to the polypeptides encoded by SEQ ID NO. 1 or SEQ ID NO. 2. Applicants also assert that the case law cited in the Office Action relates to situations where the applicant was claiming the polypeptides or polynucleotides. Applicants also argue that the written description provided is adequate because the specification describes analyzing for the expression of the polypeptides either with antibodies or with hybridization probes.

6. In response, applicants' arguments have been fully considered, but they are not persuasive. It is respectfully pointed out that it is irrelevant whether the claims are drawn to the polypeptides themselves, or to methods that assay the expression level of the polypeptides. In either case, the specification must have an adequate description of a representative number of

species, in this case polypeptides, encompassed by the claims. As indicated previously, the claims encompass analyzing the expression of polypeptides that are 90% (in some claims 95%) or more identical to the polypeptides encoded by SEQ ID NO. 1 or SEQ ID NO. 2. In this case, order to perform the claimed method, one must be able to assay for the expression of the polypeptides encompassed by the claims. However, in order to be able to analyze the expression of the polypeptides that have the desired function, the polypeptides must first have been identified—or at least the elements which are critical for the function of the polypeptides must be identified, such that it would be apparent which polypeptides that are 90% or more identical to the polypeptides encoded by SEQ ID NOS. 1 or 2 would be functional variants and which would not be functional. Here, the specification does not describe any variants of the polypeptide encoded by SEQ ID NO. 1 or 2 that retain uncoupling functions. It is also pointed out that the claims encompass analyzing the expression of polypeptides that are 90% or more identical to the polypeptide encoded by SEQ ID NO. 1 or 2, regardless if the variant polypeptides retain the uncoupling function of the wild-type polypeptide. In the cases where the polypeptides encompassed by the claims do not retain the uncoupling function of the wild-type polypeptide, the method is not enabled because the method would not necessarily identify a compound that affects uncoupling because the variant polypeptide whose expression is analyzed may not be involved in uncoupling. It is acknowledged that the specification discloses methods of analyzing polypeptide expression using antibodies and hybridization probes, however, simply being able to analyze the expression level of a polypeptide does not overcome the written description requirement for those polypeptides. For instance, merely being able to assay the presence and level of a polypeptide in a sample does not indicate which polypeptides that are assayed have the

same function of the wild-type polypeptide, which is required in order for the assay to identify compounds that affect uncoupling. As previously indicated, there is no description detailing the critical structural elements which confer uncoupling function to the polypeptides encompassed the claims. Without a clear indication of structural elements that are critical to the uncoupling function of the polypeptides encompassed by the claims, the written description requirement is not met, regardless if the polypeptides encompassed by the claims can be measured by assays using antibodies or hybridization probes. This is because the specification has not adequately described which variant polypeptides encompassed by the claims have the function required for the assay to work (uncoupling activity) and which variant polypeptides do not have the required function.

Miscellaneous

The rejection of claims under 35 USC 112, second paragraph has been withdrawn in view of the claim amendments.

The rejection of claims 59-73 under 35 USC 112, first paragraph enablement, with respect to the claims encompassing membrane potential other than mitochondrial membrane potential, has been withdrawn in view of the claim amendment limiting the claims to mitochondrial membrane potential. However, the rejection of claims under 35 USC 112, first written description, as it applies above, is maintained for the reasons herein.

Claim Objections

7. Claims 39, 40, 57, 58, 72 and 73 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims such that the claims were limited to analyzing the expression of the polypeptide encoded by SEQ ID NO. 1 or SEQ ID NO. 2.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (571) 272-0756. The examiner can normally be reached on M-F (8:00-5:30) with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

J. Eric Angell, Ph.D.
Art Unit 1635

DAVE T. NGUYEN
PRIMARY EXAMINER